Pseudo-Cushing's Syndrome in a HIV Patient with Complete Resolution Following Discontinuation of Darunavir/Ritonavir

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Introduction:

Cushing's syndrome (CS) has been reported secondary to an interaction between inhaled/intranasal fluticasone and low dose ritonavir as well as other protease inhibitors (PIs) which results in steroid accumulation, adrenal suppression and florid CS.[1-4]

There are 4 case reports of pseudo-Cushing's syndrome (p-CS) in patients taking PIs though definitive causality could not be determined as therapy was maintained in the interest of virologic control.[5]

To our knowledge, p-CS in a HIV- infected patient secondary to darunavir/low dose ritonavir with complete resolution following their discontinuation has not been reported.

Case Report:

This is a 37 year old female who was started on highly active antiretroviral therapy (HAART) with maraviroc, darunavir, low dose ritonavir and raltegravir on 02/19/2008 (CD4-253 cells/ml / HIV viral load-17,200copies/ml). At 3 weeks CD4 was 446 cells/ml with viral load down to 693 copies/ml. At that time she complained of low grade fever, sinus congestion with maxillary pain, cough and headache. This resolved s/p courses of TMP/ sulfa and levofloxacin.

On 07/11/2008 she reported 6 pound weight gain with new central adiposity and mild diffuse alopecia.

Nasal fluticasone was discontinued 07/30/2008 when she reported significant abdominal obesity with breast/posterior cervical fat pad enlargement and appearance of fat loss in her extremities. A week later she required hospital admission for insulin therapy for new onset diabetes mellitus type 2. On 08/07/2008 a dramatic change in her appearance was noted with facial plethora, bilateral parotid fullness, supraclavicular and posterior cervical fat pad enlargement and central adiposity. She noted easy bruisability and was diagnosed with oral candidiasis. On 09/02/2008 she required insulin adjustment for hemoglobinA1C of 9.3%.

On 09/08/2008 she reported ongoing substernal, non radiating chest discomfort with facial flushing, palpitations and shortness of breath. Work up ruled out pheochromocytoma and carcinoid.

The diagnosis of true CS was excluded by an endocrinologist with a normal 24 hour urine cortisol and dexamethasone suppression test.

On 10/02/2008 after a lengthy discussion with the patient all HAART medications were stopped.

On 10/21/2008 she reported feeling well with marked improvement in her Cushingoid appearance. By 11/11/2008 she was off insulin with hemoglobinA1C down to 6.3%.

On 12/11/2009 she was started on maraviroc, raltegravir and etravirine. She has had no recurrence of symptoms, despite resumption of maraviroc and raltegravir, 2 of the 3 active agents in the regimen she was on when her symptoms first occurred.

Discussion:

It is vital that p-CS secondary to PIs therapy is not missed as many of the signs/ symptoms are similar to lipodystrophy and metabolic disease associated with HIV and HAART and it is likely to resolve after discontinuation of the causal agent as in this case. Further studies are required to determine if darunavir is more likely than other PIs to cause this syndrome.

References:

1 Clevenbergh P, Corcostegui M, Gerard D,Hieronimus S,Mondain V,Chichmanian RM,Sadoul JL,Dellamonica P. Iatrogenic Cushing's syndrome in an HIV-infected patient treated with inhaled corticosteroids (fluticasone propionate) and low-dose ritonavir-enhanced PI-containing regimen. J Infect April 2002; 44(3):194–195.

2 Nadia Valin, Nathalie De Castro,Valerie Garrait,Anne Bergeron, Clara Bouche, Jean Michel Molina. Iatrogenic Cushing's Syndrome in HIV-Infected Patients Receiving Ritonavir and Inhaled Fluticasone: Description of 4 New Cases and Review of the Literature. Journal of International Association of Physicians AIDS Care (Chic Ill).2009; 8: 113-121.

3 St.Germain RM, Yigit S, Wells L, Giratto JE, Salazar JC.Cushing's syndrome and severe adrenal suppression caused by fluticasone and protease inhibitor combination in an HIV-infected adolescent. AIDS Patient Care STDs 2007; 21:373–377.

4 MM Foisy, 1, 2 EMK Yakiwchuk,2 I Chiu3 and AE Singh3. Adrenal suppression and Cushing's syndrome secondary to an interaction between ritonavir and fluticasone: a review of the literature. 2008 British HIV Association HIV Medicine. 2008: 9; 389–396.

5 Karen K. Miller, Patricia A. Daly, Deborah Sentochnik, John Doweiko, Matthew Samore, Nesli O. Basgoz and Steven K. Grinspoon Pseudo-Cushing's Syndrome in Human Immunodeficiency Virus-Infected Patients Clinical Infectious Diseases: July,1998; Vol. 27, (1),pp. 68-72.